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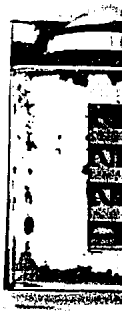

ANIMAL NEUROVIRUS DISEASES SIMILAR TO HUMAN POLIOMYELITIS

Zhurnal Nevropatologii i Psikhiatrii,
Vol 53, No 8, pp 648-652
Moscow, Aug 1953

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The absence of a satisfactory laboratory model of poliomyelitis makes the experimental study of this disease extremely difficult.

At present, the only method of detecting the poliomyelitis virus is the experimental infection of monkeys or apes (obyez'yany) by means of virus-containing material obtained from the brains of dead human beings or the excrement of afflicted persons. The higher apes (such as chimpanzees) seem to be the most receptive to this method, followed by Javanese macaques, rhesus monkeys, hamadryas baboons, and green guenons, in that order. Increased interest in research pertaining to the study of the possibility of adapting the poliomyelitis virus to other species of animals is, therefore, understandable.

As yet, only a few strains of the poliomyelitis virus have been successfully adapted to white mice and cotton rats (Sigmodon hispidus). This refers to Lansing "SK," "K," "MM," Levkovich "113," and others.

In recent years a great deal of attention has been given to neuroinfections of animals which are similar to human poliomyelitis. At present, their epidemiological significance in the dissemination of poliomyelitis has not yet been established. These poliomyelitis-like infections of animals, however, are of undoubted scientific and practical interest to the medical world. Encephalomyelitis of mice and enzootic paralysis of swine (the Teschen disease) are two such infections.

The virus of encephalomyelitis of mice was isolated in the Soviet Union by I. A. Shifrin, L. Ya. Yablonovskaya, and others.

The particles of the virus which causes the disease in mice have extremely small dimensions, approximating the dimensions of the virus of human poliomyelitis. The mouse virus, it has been found, affects primarily the cells of the spinal cord. It is very stable, and can be preserved for several weeks or even months. Seriological investigations of mice to detect antibodies did not give accurate results. Contradictory data likewise were obtained in experiments attempting to determine the presence of specific immunity in mice after they had been infected intracerebrally. These characteristics of the virus of encephalomyelitis of mice in many ways closely resemble the properties of the virus of human poliomyelitis.

Despite the similarity of these viruses, however, there is no basis whatsoever for assuming that mice or any other animals act as a reservoir of the poliomyelitis virus.

To clarify this question, it will be necessary to carry out investigations, since information concerning the spread of the virus of mouse encephalomyelitis is very meager and the relationships of this virus to the virus of human poliomyelitis so far have not been adequately studied.

A number of authors have pointed out the great similarity of human poliomyelitis to the Teschen disease of swine. This disease was first described by Trefni (1930-1931) in the Teschen district of Czechoslovakia, from which it received its name. It next became widespread in the Sudeten region, Bohemia, and Moravia. It was recorded in the border regions of Bavaria, Austria, and Central Germany (Leipzig). Spreading further, the disease affected the northeastern districts of Slovakia and then penetrated into Hungary, Yugoslavia, Switzerland, and Italy.

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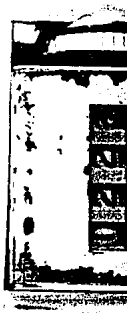

Comparatively recently, in 1950, Lepine and Apanasiou isolated on Madagascar a virus causing encephalomyelitis of swine. This virus turned out to be identical with the Czechoslovakian strain of the virus of Teschen disease. It is pathogenic exclusively for domesticated and wild swine. Monkeys and apes, hamsters, mice, guinea pigs, and rabbits are not susceptible to intracerebral infection with this virus. Blood serum of recovered animals neutralizes both the Madagascar and Czechoslovakian strains to a certain degree. At the same time, the virus of the Teschen disease does not prevent mice from becoming ill when they are infected with a Lansing-type strain of poliomyelitis.

According to the data of Klobouk, Fortner and others, the virus [of Teschen disease] passes through a Berkefeld N filter. Consequently, the dimensions of its particles are approximately the same as those of the poliomyelitis virus. It is very stable, can be preserved for 20 or more months in glycerine, does not lose its virulence for 3 months when stored at a temperature of minus 15°, withstands drying in the sun for 23 days, and does not perish in a brine solution at minus 6° to minus 10° or in putrescent material for about 6 days. The virus is inactivated in 30 minutes at a temperature of plus 70°.

The virus cannot be cultured in chicken embryos and does not infect chicks which have just hatched (Gallia, 1949). Under natural conditions, outside a living organism, it preserves its virulence for a long time.

The virus is detected in large quantities in the central nervous system at the start of the illness, especially during the first few days after the appearance of paresis and paralysis. Less regularly, it appears in the various secretions and excretions of the mucous membrane of the nasopharynx. A clinical case of the disease cannot be induced by artificial infection with blood or a suspension made from organs that contain blood.

Only domesticated and wild swine, and then primarily young animals, have been successfully infected. The basic sources of the infection are, evidently, sick animals with either a manifest or hidden form of the disease and animals which have recovered but still remain carriers and transmitters of the virus for a long time after their recovery. Under natural conditions, infection occurs mainly through the alimentary tract and the nasal passage. Under specific external conditions (severe changes in the weather, dampness, cold weather, or weakness brought about by a vaccination or surgical operation) susceptibility to the disease increases significantly.

Young pigs who have lived through the natural disease become immune, but some cases have been recorded in which the animals were reinfected or even died. Some authors look upon this as proof that several types of the virus of the Teschen disease exist. By subcutaneous and intravenous injections of the living virus an active immunity can be developed. Individual animals can be made to incur a clinical form of encephalitis by feeding them on infected matter.

The use of vaccines for prophylactic purposes is limited in effectiveness, since the immunity develops approximately 30 or 40 days after inoculation and then lasts for no more than 2 to 4 months.

The cited characteristics of the properties of the virus which causes the Teschen disease in young pigs are similar in many ways to the characteristics of the virus of human poliomyelitis. The immunological behavior of the two viruses is different, however.

Comparisons of clinical poliomyelitis-like animal diseases with human poliomyelitis are of some interest. Gard in 1943 and Kaplan and Merentze in 1948 pointed out the unusual similarities of the Teschen disease of swine and encephalomyelitis of mice to human poliomyelitis.

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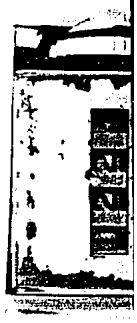

Both in poliomyelitis and the Teschen disease the preparalytic stage of the illness is characterized by fever and meningeal phenomena (there is no information concerning encephalomyelitis of mice). The paralytic stage is much the same in all three diseases: flaccid paralysis is observed, primarily of the extremities, and cerebral forms appear, accompanied by ataxia and spastic symptoms, or tonic and clonic spasms.

Nonparalytic forms of all three infections have been recorded. The incubation period in an experimental infection lasts from 10 to 14 days. The disease can occur in an abortive form, resulting in full recovery without the development of paralysis. Some similarity can also be detected in the pathological changes, but there is an essential difference, which is especially apparent when a study is made of the dynamics of the pathohistological changes.

All three of these disease-causing agents are distinguished, as is shown above, by a typical species characteristic. Furthermore, they primarily affect young individuals. The diseases also are characteristically seasonal; the greatest incidence of the disease is recorded in the spring. On the other hand, each of the diseases being compared has its own peculiarities and variations, which establish a basis for considering the Teschen disease and encephalomyelitis of mice as independent diseases not related to human poliomyelitis.

Reports recently have appeared concerning the possibility of using antigens obtained from the virus of the Teschen disease for the laboratory diagnosis of poliomyelitis. Semenits and Rush in 1950, basing their work on the similarity of the Teschen disease of mice [this should possibly be of swine] to human poliomyelitis, prepared in a corresponding manner an antigen from the brain matter of young pigs which had died of the Teschen disease. They then used this antigen to set up a reaction of complement fixation in spinal fluid obtained from children ill with poliomyelitis.

Semenits and Rush confirmed a diagnosis of poliomyelitis in 57 children. In 23 children and adults suffering from serous meningitis, the complement-fixation reaction was negative. Negative results were also obtained when the reaction was set up with 60 control samples of spinal fluid from persons suffering from tuberculous meningitis, spinal atrophy, meningococcal infection, etc..

There are references in literature to the existence of poliomyelitis-like diseases in other domestic animals. Thus, for example, Frauhiger, in 1938, reported such a disease affecting calves during a poliomyelitis epidemic in Switzerland. The illness of the calves resembled Landry's ascending spinal paralysis with the affliction first in the rear and then in the front extremities. Changes detected in the spinal chord of the animals were similar to those recorded in human poliomyelitis These changes were most evident in the lumbar and sacroiliac regions. They consisted of a perivascular infiltration by leukocytes and plasmocytes, especially into the forward vertebral processes, and of the destruction of ganglionic cells accompanied by phenomena of neuronophagy.

In 1938, Frauhiger and Hofman succeeded in experimentally infecting three calves with the poliomyelitis virus. They did this by simultaneously injecting into their brains, noses, and abdominal cavities of the calves a suspension containing the infectious agent. The animals incurred paralysis in their extremities.

Ferlicus observed a poliomyelitis-like disease in dogs in 1950.

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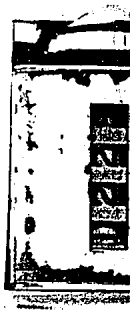

Proceeding from these data, and considering poliomyelitis from the evolutionary-ecological point of view, several authors have expressed the hypothesis that in nature there exists a whole group of poliomyelitis-like viruses, which may have one common ancestor. It remains unclear, however, what the first host organism for the poliomyelitis virus was — human or animal.

An assumption was also made that the poliomyelitis virus developed as an intestinal parasite of rodents, without perhaps causing a clinical infection in them. However, the virus gradually evolved and at some point became pathogenetic for human beings. The causes for this change in its pathogenetic properties remain unclear. Several authors, for instance, Barnet, suggested that the origination of new strains with increased virulence might be explained by mere chance.

However, "Science is the enemy of chance. Science can only really be called science, when it discovers the laws governing development" [T. D. Lysenko, according to M. B. Mitin, For a Materialistic Biological Science (Za Materialisticheskuyu Biologicheskuyu Nauku), p 103, Moscow-Leningrad, 1949]. Doubtlessly, the solution of this complicated problem is only possible on the basis of Michurin's biology, which regards the mutability of microbes and viruses as a result of changes in environmental conditions.

Proceeding from the similarity between the Teschen disease and human poliomyelitis, we attempted, in 1950, to infect young pigs with several strains of poliomyelitis. To 12 young pigs was administered a massive dose (1 ml into the brain, 20 ml into the abdominal cavity, and 3 ml into the nose) of six strains of poliomyelitis virus: Kvade, strain "113," KRF-1, MV, I-16, and Shevk. Two young pigs were used for each strain. The animals remained healthy. In some of them there was an insignificant rise in temperature, but this was not accompanied by any clinical manifestation of the disease whatsoever. One of the young pigs which had been infected with the I-16 (Lansing) strain and had had no clinical manifestation of the disease was killed 13 days after the attempted infection. A suspension of brain tissue from this pig was used to infect a monkey and two other young pigs. None of them became diseased.

Thus, attempts to adapt human poliomyelitis to young pigs were fruitless. An attempt to cause a monkey to become ill by infection with a massive dose (1 ml into the brain, 10 ml into the abdominal cavity, and 3 ml into the nose) of the Czechoslovakian strain of the Teschen disease was likewise unsuccessful, although the simultaneous infection of a young pig with this virus caused it to fall ill, and, subsequently, to die on the 10th day after the infection.

After successful preliminary passages of a strain of the virus of the Teschen disease, we set up a titration experiment with the virus. Ten young pigs were injected with diluted solutions of a brain suspension obtained from animals which had died. The dilution ranged from 1:10 to 1:10,000. Titration of the virus showed that intracerebral infection of the young pigs with a 0.5 ml dose was possible with dilutions as high as 1:1,000. One out of two of the young pigs became ill, and at the same time, the incubation period for the disease was extended to 14 days.

A comparison of various methods of infecting young pigs with the Teschen disease is of undoubted interest. For this purpose we produced infection by injection into the brain, the nose, the tonsils, and also intracutaneously. In the last method, 0.05-ml doses of the virus were injected at ten points on the hind feet. Intracutaneous infection was repeated every week, just as we did in the intracutaneous infection of monkeys and apes with poliomyelitis virus (Rodin, Itselis, 1951).

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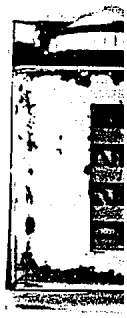

All the young pigs infected by injection into the brain became ill in 5-9 days. We succeeded in causing the disease in one of the two young pigs infected by injecting the virus into the tonsils. Intracutaneous infection caused the disease in one of the two young pigs infected. On the 5th day after the second intracutaneous injection of the virus, the pig's temperature increased sharply and the animal soon developed a flaccid paralysis of the legs, particularly the front ones.

The infection of two young pigs by injection into the nose, 1.5 ml in each nostril, was likewise successful.

The clinical pattern of the disease following experimental infection of young pigs with the Teschen virus, despite differences in the individual neurological symptoms, is generally quite uniform. It comprises nystagmus, convulsive movements, trembling of the whole body (especially the head), opisthotonus, ataxia, and weakness of all the legs, usually without paralysis. Flaccid paralysis of the extremities developed in only two of the young pigs, one infected through the nose and the other intracutaneously.

Simultaneously with the infection of the young pigs with the Teschen virus, white mice, cotton rats, and guinea pigs were repeatedly, but unsuccessfully, injected with the virus.

Our investigations show that the Teschen disease of swine is characterized by the duration of the incubation period, which almost never varies in length subsequently to intracerebral experimental infection. The length of the incubation period changes somewhat depending on the means of infection and the degree of dilution of the virus. According to our data, the majority of young pigs infected by injection into the brain become ill in 6-7 days, whereas those infected by injection into the nose, the tonsils, or intracutaneously exhibit an incubation period of 11-12 days.

This constancy of the length of the incubation period with the same method of infection, and the constancy of the clinical symptoms, which are clearly pronounced, afford us the possibility of using our observations on the Teschen disease for the solution of some of the problems of pathogenesis and immunity in neuroinfections.

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